Session II

Nicotinergic Receptors in Neurodegenerative Disorders

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NICOTINIC RECEPTORS IN THE BRAIN : MOLECULAR BIOLOGY, FUNCTION AND THERAPEUTICS

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Although the psychological and physiological effects of nicotine have long suggested that nicotine excerts specific actions in the brain, the identification of neuronal nicotinic receptors (nAChRs) only began in the past few years with the development of molecular genetics approaches. It is now clear that, unlike muscle nAChRs, the neuronal nAChRs are composed of a large diversity of molecular entities. In fact, neuronal nAChRs form a family of highly heterogenous receptor subtypes, as evidenced by the number of genes encoding nAChR subunits, the diversity of immuno-purified receptor proteins and the multiple functional types of ligand-gated ion channels. Neuronal nAChRs have discrete localizations within the brain and are involved in modulating neuronal firing and transmitter release. Cumulative evidence from animal and human studies indicate that nicotinic systems play a major role in higher cognitive functions and dysfunctions (cf Vidal, C., 1994, Drug Develop. Res., 31, 120-126). In particular the loss of cortical nAChRs appears as a neurochemical hallmark of Alzheimer's (AD) and Parkinson's (PD) disease. Pilot clinical studies have shown that nicotine improves learning and memory performances in AD and PD. Although specific functions have yet to be ascribed to the different types of nAChRs in the brain, the use of nicotinic compounds appears as a promissive approach in the treatment of senile dementias.

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